

Original Article

Actual treatments for out-of-hospital ventricular fibrillation at critical care medical centers in Osaka: a pilot descriptive study

Tomohiko Sakai,¹ Tetsuhisa Kitamura,² Taku Iwami,² Yasuyuki Hayashi,³ Hiroshi Rinka,⁴ Yasuo Ohishi,⁵ Tomoyoshi Mohri,⁶ Masafumi Kishimoto,⁷ Ryosuke Kawaguchi,⁸ Kentaro Kajino,⁹ Tetsuya Yumoto,¹⁰ Toshifumi Uejima,¹¹ Masahiko Nitta,¹² Tatsuya Nishiuchi,¹³ Chizuka Shiokawa,¹⁴ Taro Irisawa,¹ Osamu Tasaki,¹ Hiroshi Ogura,¹ Yasuyuki Kuwagata,¹ and Takeshi Shimazu¹

¹Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School of Medicine, Osaka; ²Kyoto University Health Service, Kyoto; ³Senri Critical Care Medical Center, Saiseikai Senri Hospital, Suita; ⁴Emergency and Critical Care Medical Center, Osaka City General Hospital, Osaka; ⁵Osaka Mishima Emergency Critical Care Center, Osaka; ⁶Critical Care and Trauma Center, Osaka General Medical Center, Osaka; ⁷Osaka Prefectural Nakakawachi Medical Center of Acute Medicine, Higashi-Osaka; ⁸Osaka Prefectural Senshu Critical Care Medical Center, Izumi-Sano; ⁹Emergency and Critical Care Medical Center, Osaka Police Hospital, Osaka; ¹⁰Traumatology and Critical Care Medical Center, National Hospital Organization Osaka National Hospital, Osaka; ¹¹Department of Emergency and Critical Care Medicine, Kinki University School of Medicine, Osaka-Sayama; ¹²Department of Emergency Medicine, Osaka Medical College Hospital, Takatsuki; ¹³Department of Critical Care and Emergency Medicine, Osaka City University Graduate School of Medicine, Osaka; ¹⁴Osaka Prefectural Council of Emergency Care Facilities, Osaka, Japan

Aim: Although advanced treatments are provided to improve outcomes after out-of-hospital ventricular fibrillation, including shock-resistant ventricular fibrillation, the actual treatments in clinical settings have been insufficiently investigated. The aim of the current study is to describe the actual treatments carried out for out-of-hospital ventricular fibrillation patients, including shock-resistant ventricular fibrillation patients, at critical care medical centers.

Methods: We registered consecutive adult patients suffering bystander-witnessed out-of-hospital cardiac arrest of cardiac origin, for whom resuscitation was attempted by emergency medical service personnel, who had ventricular fibrillation as an initial rhythm, and who were transported to critical care medical centers in Osaka from March 2008 to December 2008. This study merged data on treatments after transportation, collected from 11 critical care medical centers in Osaka with the prehospital Utstein-style database.

Results: During the study period, there were 260 bystander-witnessed ventricular fibrillation arrests of cardiac origin. Of them, 252 received defibrillations before hospital arrival, 112 (44.4%) were transported to critical care medical centers, and 35 had shock-resistant ventricular fibrillation. At the critical care medical centers, 54% (19/35), 40% (14/35), and 46% (16/35) of shock-resistant ventricular fibrillation patients were treated with extracorporeal life support, percutaneous coronary interventions, and therapeutic hypothermia, respectively, but their treatments differed among institutions. Some patients with prolonged arrest without prehospital return of spontaneous circulation who received advanced treatments had neurologically favorable survival, whereas approximately two-thirds of shock-resistant ventricular fibrillation patients with advanced treatments did not.

Conclusion: This pilot descriptive study suggested that actual treatments for prehospital ventricular fibrillation patients differed between critical care medical centers. Further studies are warranted to evaluate the effectiveness of in-hospital advanced treatments for ventricular fibrillation including shock-resistant ventricular fibrillation.

Key words: Advanced life support (ALS), extracorporeal life support, hypothermia, out-of-hospital cardiac arrest, ventricular fibrillation

Corresponding: Taku Iwami, MD, PhD, Kyoto University Health Service, Yoshida Honmachi, Sakyo-ku, Kyoto 606-8501, Japan. E-mail: iwamit@e-mail.jp.

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INTRODUCTION

OUT-OF-HOSPITAL CARDIAC ARREST (OHCA) of cardiac origin is one of the leading causes of death in the industrialized world,¹ with approximately 70,000 events occurring every year in Japan.² However, survival after OHCA is still low.

Recently, we reported that the annual incidence of prehospital shock-resistant ventricular fibrillation (VF) patients, who had sustained VF at hospital arrival and needed advanced treatments in addition to prehospital care, has remained unchanged and their outcomes were still dismal.³ We also suggested that the transportation of OHCA patients to the critical care medical centers (CCMCs) was associated with better outcomes after OHCA.⁴ Some reports suggested the effectiveness of extracorporeal life support (ELS) usage before return of spontaneous circulation (ROSC),^{5,6} and in-hospital post-arrest care such as therapeutic hypothermia (TH)^{7,8} and percutaneous coronary intervention (PCI)⁹ to improve the outcome after OHCA. However, actual advanced treatments carried out for VF at CCMCs, including shock-resistant VF patients who would especially need to receive advanced treatments, has been insufficiently investigated.

The Utstein Osaka Project, begun in 1998, is a large, ongoing, prospective, population-based cohort study of OHCA in Osaka Prefecture, Japan, covering a population of 8.8 million.¹⁰ In this study, we extracted detailed in-hospital records on actual treatments at CCMCs, and merged them with the data on resuscitation simultaneously collected based on the Utstein-style guidelines.¹¹ The aim of this study was to describe the present conditions of treatments for VF at the CCMCs in Osaka, one of Japan's most developed areas of prehospital emergency medical service (EMS) systems.¹⁰ In particular, we focused on the conditions of shock-resistant VF.

METHODS

Population and setting

THE TARGET AREA for this study was Osaka Prefecture in Japan, which has an area of 1,897 km² and a residential population of 8,817,166 inhabitants in 2005.¹² Males make up 48.5% of the population, 18.5% of who are aged 65 years or older.

Osaka Prefecture included 541 hospitals (109,503 beds) in 2008.¹³ Of them, 269 including 13 CCMCs can accept emergency cases of severely ill patients, including OHCA cases, from ambulances.¹⁴ As many as 30% of OHCA patients in Osaka Prefecture were transported to CCMCs and then treated.⁴ In this study, 11 of 13 CCMCs in Osaka participated in our registry.

Study patients

From March 8, 2008 to December 31, 2008 we registered consecutive patients aged ≥ 18 years suffering OHCA of presumed cardiac origin, who were witnessed by bystanders and for whom attempted resuscitation was attempted by EMS, who had VF as an initial rhythm, and were then transported to CCMCs. The Ethics Committee of Osaka University Hospital (Osaka, Japan) approved this study as the principal institution, and after the approval each hospital individually approved our study protocol as necessary. The requirement of giving individual informed consent for the review of patient outcomes was waived by the Personal Information Protection Law and the national research ethics guidelines of Japan.

Emergency Medical Service organization and equipment in metropolitan Osaka

The 119 emergency telephone number is accessible anywhere in Japan. On receipt of a 119 call, an emergency dispatch center sends the nearest available ambulance to the site. These dispatch centers are operated by each fire station managed by the municipal government; 34 fire stations with a dispatch center were located across this catchment area in 2008. Each ambulance includes a three-person unit providing life support 24 h a day. Most highly trained EMS personnel are called emergency life-saving technicians. They are allowed to insert an i.v. line and an adjunct airway and to use a semi-automated external defibrillator for OHCA patients. Emergency life-saving technicians were permitted to provide shocks without consulting a physician from 2003. Specially trained emergency life-saving technicians were allowed to carry out tracheal intubation and to administer epinephrine for OHCA patients. All EMS providers carried out cardiopulmonary resuscitation (CPR) according to the 2005 Japanese CPR guidelines during this study period.¹⁵ Details of the EMS systems in Osaka were described previously.¹⁰

Data collection and quality control

Data were collected prospectively with the use of a data form based on the Utstein-style international guideline of reporting OHCA, including age, gender, origin of cardiac arrest, location of cardiac arrest, initial cardiac rhythm, bystander-initiated CPR, activities of daily living before arrests, and prehospital time-course of resuscitation, as well as ROSC, 1-month survival, and neurological status 1 month after the event.¹¹ Initial rhythm was recorded and diagnosed by EMS personnel with semi-automated defibrillators on the scene. A data form was filled out by EMS personnel in cooperation

with the physicians in charge of the patient, transferred to the Information Center for Emergency Medical Services of Osaka, and then checked by the investigators. If the data sheet was incomplete, the relevant EMS personnel were interviewed and the data sheet completed.

All survivors were followed for up to 1 month after the events by the EMS personnel in charge. Neurological outcomes 1 month after the events were determined by the physician responsible for the care of the patient, using the Cerebral Performance Category (CPC) scale: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; category 5, death.¹¹ The primary outcome measure was neurologically favorable 1-month survival. Neurologically favorable outcomes were defined as CPC categories 1 or 2.¹¹

In-hospital data were also prospectively collected using an original report form by the physician in charge of the patient at each CCMC. The report form required the following data on the actual treatments and their resuscitation time-courses; anti-arrhythmic drug therapies (amiodarone, nifekalant, and lidocaine), tracheal intubation, ELS, cardioangiography and PCI, and TH within 1 week after the transportation of OHCA patients to the CCMCs. These data were merged with the data based on the Utstein-style guidelines by the principal investigators.

Definition of shock-resistant VF

Ventricular fibrillation or pulseless ventricular tachycardia (VT) as an initial rhythm that persisted upon hospital arrival following at least one preceding EMS' electrical shock was defined as shock-resistant VF.³

Statistical analysis

Patient and EMS characteristics were compared between the groups using ANOVA for numerical variables and the χ^2 -test for categorical variables. All the tests were two-tailed, and *P*-values of <0.05 were considered statistically significant. All statistical analyses were carried out using the SPSS statistical package version 16.0J (SPSS, Inc., Chicago, IL, USA).

RESULTS

FIGURE 1 SHOWS AN overview of study patients based on the Utstein template. A total of 5,289 adult OHCA patients were documented during the study period. Among them, 4,917 were resuscitated, and 1,080 were witnessed by bystanders. Among the witnessed cases, 260 (24.1%) had VF

including pulseless VT, 355 (32.9%) pulseless electrical activity (PEA), and 443 (41.0%) asystole as prehospital initial rhythm. Data on the initial rhythm was not applicable for 22 (2.0%) cases. Among 260 initial VF arrests, 252 (96.9%) were delivered at least one shock by EMS personnel before hospital arrival. Of them, 112 (44.4%) were transported to CCMCs, and were eligible for our analyses. Among the 112 CCMC treated cases, 43 (38.4%) had prehospital ROSC, 35 (31.3%) persisting VF, 17 (15.2%) PEA, and 17 (15.2%) asystole at hospital arrival.

Demographic and resuscitation characteristics among prehospital VF patients according to their cardiac rhythm at CCMC arrival are noted in Table 1. Patient characteristics were similar between the groups. The proportion of bystander-initiated CPR was lower in the PEA group than the other groups (*P* = 0.040). The mean time intervals from collapse to call and hospital arrival showed no significant differences between the groups. The mean time intervals from collapse to EMS arrival at the scene (*P* = 0.013) and first shock (*P* = 0.004) were shorter in the ROSC group than in the other groups.

Table 2 shows the outcomes among prehospital VF patients according to the cardiac rhythm at CCMC arrival. With regard to 112 patients transported to CCMCs, the proportion of neurologically favorable 1-month survival among those with ROSC before hospital arrival, persisting VF, PEA, and asystole was 65.1% (28/43), 28.6% (10/35), 11.8% (2/17), and 11.8% (2/17), respectively.

Table 3 shows the present conditions of advanced treatments for prehospital VF patients according to their cardiac rhythm at CCMC arrival. Among VF cases at CCMC arrival, amiodarone and nifekalant were used for 40.0% (14/35) and 45.7% (16/35) cases, respectively. Tracheal intubation was carried out for all cases, and TH was carried out for 60.5% (26/43) among the ROSC group, 45.7% (16/35) VF, 23.5% (4/17) PEA, and 17.6% (3/17) asystole group. Figure 2 shows the time-series of advanced treatments against shock-resistant VF cases according to CCMCs. A total of 35 shock-resistant VF patients were transferred to eight CCMCs from the scene. At the CCMCs, 54.3% (19/35), 40.0% (14/35), and 45.7% (16/35) of shock-resistant VF patients were treated with ELS, PCI, and TH, respectively. The introduction and timing of anti-arrhythmic drug administration, ELS, PCI, and TH, and termination of resuscitation (TOR) for these patients differed exceedingly between CCMCs. At one CCMC (Hospital H), no shock-resistant VF patients received any advanced treatments excluding amiodarone. Two cases in Hospitals A and C with prolonged resuscitation of ≥ 60 min after collapse who received advanced treatments including TH, ELS, and PCI had neurologically favorable survival, whereas approximately two-thirds (17/27) of

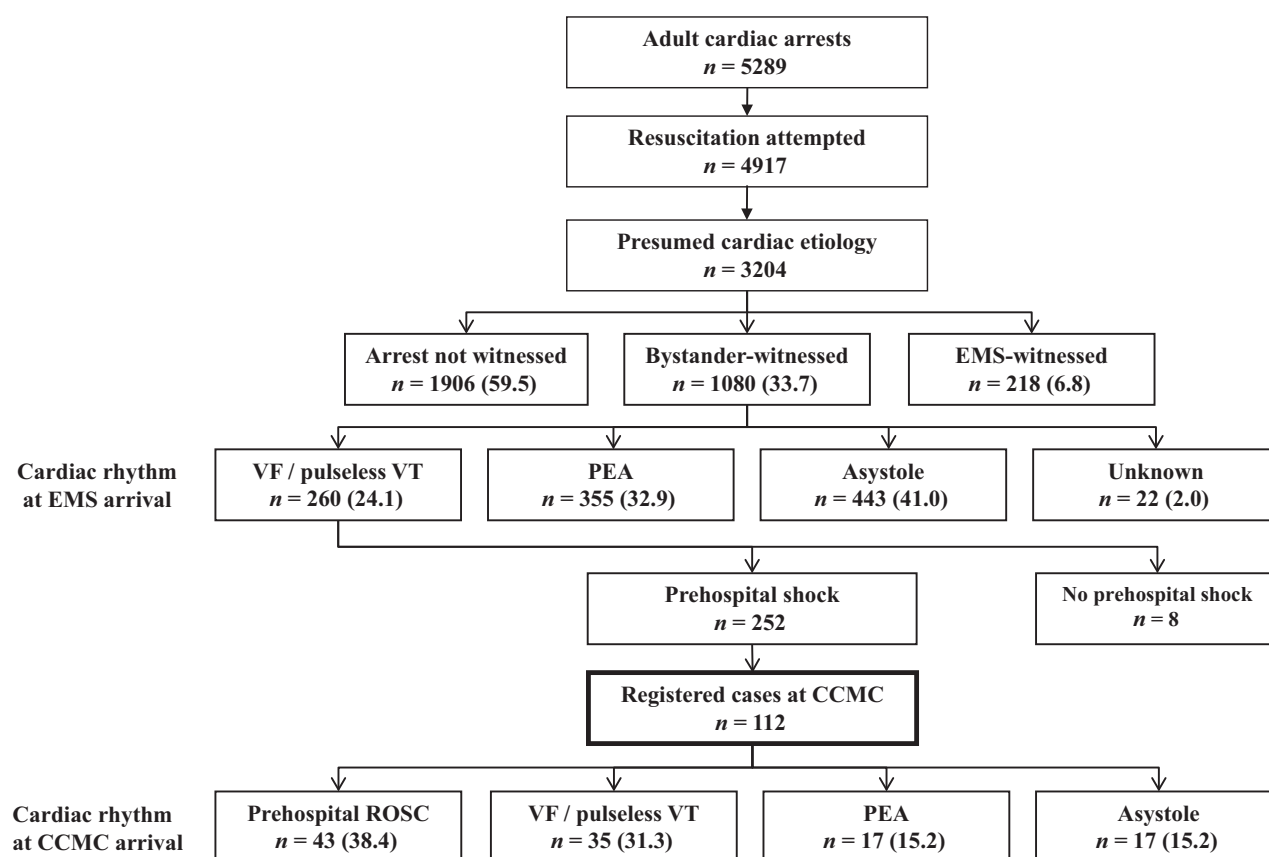


Fig. 1. Overview of emergency medical service (EMS)-treated cardiac arrests in Osaka Prefecture with an abridged Utstein template (March 8, 2008–December 31, 2008). Values in parentheses are mean percentages. CCMC, critical care medical center; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; VT, ventricular tachycardia.

Table 1. Characteristics of ventricular fibrillation (VF) patients at emergency medical service (EMS) arrival according to cardiac rhythm on critical care medical center arrival

	ROSC (n = 43)	VF/VT (n = 35)	PEA (n = 17)	Asystole (n = 17)	P-value
Age, year, mean (SD)	62.7 (14.0)	60.2 (13.4)	60.3 (17.1)	63.1 (14.5)	0.826
Gender, male, n (%)	35 (81.4)	30 (85.7)	11 (64.7)	15 (88.2)	0.255
Location of arrests, home, n (%)	17 (39.5)	19 (54.3)	7 (41.2)	11 (64.7)	0.261
Good daily living activities before arrests, n (%)	36 (83.7)	31 (88.6)	15 (88.2)	13 (76.5)	0.683
Bystander-initiated CPR, n (%)	21 (48.8)	13 (37.1)	2 (11.8)	9 (52.9)	0.040
Epinephrine administration by EMS, n (%)	16 (37.2)	11 (31.4)	6 (35.3)	5 (29.4)	0.925
Intubation by EMS, n (%)	14 (32.6)	13 (37.1)	5 (29.4)	4 (23.5)	0.791
Collapse to call, min, mean (SD)	1.3 (2.4)	1.3 (2.0)	3.7 (7.9)	2.4 (2.7)	0.121
Collapse to EMS arrival at scene, min, mean (SD)	7.5 (2.6)	8.0 (2.7)	11.1 (7.9)	9.6 (4.0)	0.013
Collapse to first shock by EMS, min, mean (SD)	9.0 (2.5)	10.1 (2.9)	13.5 (8.7)	11.1 (3.9)	0.004
Collapse to hospital arrival, min, mean (SD)	29.6 (6.2)	31.2 (10.5)	36.1 (14.6)	31.8 (12.0)	0.178

CPR, cardiopulmonary resuscitation; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; SD, standard deviation; VT, ventricular tachycardia.

Table 2. Outcomes of prehospital ventricular fibrillation (VF) patients at emergency medical service arrival according to cardiac rhythm on critical care medical center CCMC and non-registered hospital arrival

	ROSC	VF/VT	PEA	Asystole	P-value
112 patients transported to CCMCs	(n = 43)	(n = 35)	(n = 17)	(n = 17)	
Admission, n (%)	43 (100.0)	22 (62.9)	12 (70.6)	5 (29.4)	<0.001
Survival at 1 month, n (%)	37 (86.0)	15 (42.9)	6 (35.3)	3 (17.6)	<0.001
Neurologically favorable 1-month survival, n (%)	28 (65.1)	10 (28.6)	2 (11.8)	2 (11.8)	<0.001
140 patients transported to non-registered hospitals	(n = 34)	(n = 35)	(n = 35)	(n = 36)	
Admission, n (%)	34 (100.0)	17 (48.6)	20 (57.1)	13 (36.1)	<0.001
Survival at 1 month, n (%)	30 (88.2)	9 (25.7)	10 (28.6)	2 (5.6)	<0.001
Neurologically favorable 1-month survival, n (%)	24 (70.6)	6 (17.1)	2 (5.7)	1 (2.8)	<0.001

PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VT, ventricular tachycardia.

Table 3. Conditions of treatment for 112 ventricular fibrillation (VF) patients at emergency medical service arrival according to cardiac rhythm on critical care medical center arrival

	ROSC (n = 43)	VF/VT (n = 35)	PEA (n = 17)	Asystole (n = 17)	P-value
Anti-arrhythmic drug, n (%)					
Amiodarone	5 (11.9)	14 (40.0)	1 (5.9)	0 (0.0)	<0.001
Nifekalant	3 (7.1)	16 (45.7)	2 (11.8)	6 (35.3)	<0.001
Lidocaine	5 (11.9)	12 (34.3)	3 (17.6)	6 (35.3)	0.070
Tracheal intubation, n (%)					0.634
Inserted at scene	10 (23.3)	10 (28.6)	5 (29.4)	3 (17.6)	
Inserted at hospital	30 (69.8)	25 (71.4)	12 (70.6)	13 (76.5)	
Not inserted	3 (7.0)	0 (0.0)	0 (0.0)	1 (5.9)	
Extracorporeal life support, n (%)	4 (9.3)	19 (54.3)	1 (5.9)	3 (17.6)	<0.001
Cardioangiography, n (%)	33 (76.7)	21 (60.0)	6 (35.3)	3 (17.6)	<0.001
Percutaneous coronary intervention, n (%)	13 (31.7)	14 (40.0)	3 (17.6)	1 (5.9)	0.002
Therapeutic hypothermia, n (%)	26 (60.5)	16 (45.7)	4 (23.5)	3 (17.6)	0.006

PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; VT, ventricular tachycardia.

shock-resistant VF patients who received advanced treatments did not.

DISCUSSION

THIS REGISTRY OF VF at CCMCs in Osaka suggested that approximately 30% of out-of-hospital VF patients had persistent VF at hospital arrival, and advanced treatments such as use of anti-arrhythmic drugs, ELS, PCI, and TH, and TOR for shock-resistant VF patients differed among the CCMCs even in the same area. Some hospitals provided treatments far beyond that recommended by the CPR guidelines, whereas some provided less treatment than

recommended. Advanced treatments such as ELS, PCI, and TH have been recommended for persistent VF patients,^{16,17} but, to our knowledge, few studies have investigated in detail the actual condition of treatments for shock-resistant VF patients covering a certain population.

Although the CPR guidelines recommend that comatose cardiac arrest survivors should receive TH after VF,^{1,18,19} the present study showed that the implementation of TH was quite different by institutions even in the developed area of the EMS system. In addition, it was difficult to compare the present conditions on TH because the definition of TH itself and protocol differed in each CCMC. Indeed, the implementation of TH after cardiac arrest has remained very low in the

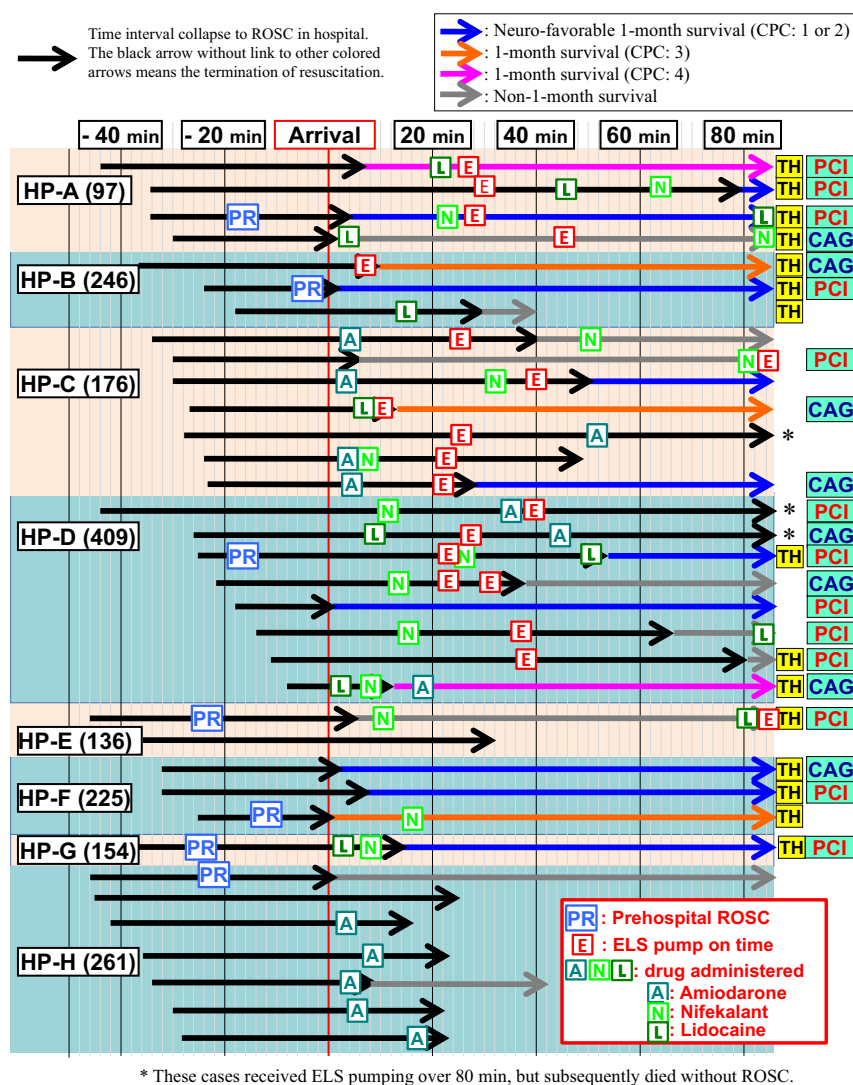


Fig. 2. Treatments for patients with shock-resistant ventricular fibrillation (VF) ($n = 35$) in eight Osaka Prefecture critical care medical centers (March 8, 2008–December 31, 2008). Each line with arrowhead indicates one shock-resistant VF patient. The number in parentheses after each hospital identifier (HP-A–H) represents the number of all out-of-hospital cardiac arrest patients transported to each hospital in 2008. The horizontal axis shows the time-course from collapse based on hospital arrival time. On the right side of the figure, TH, CAG, and PCI, indicate the actual treatments of therapeutic hypothermia, cardioangiography, and percutaneous coronary intervention, respectively, carried out for each shock-resistant VF patient. A, amiodarone; CA, cardioangiography start time; E, timing of extracorporeal life support (ELS) pump-on time; L, lidocaine; N, nifekalant; PR, prehospital ROSC.

USA,²⁰ and these findings suggest that it takes a long time to disseminate practice guidelines in real medical settings, as previously reported.^{21,22}

In this study group, approximately 50% of shock-resistant VF patients were treated with ELS. Although some published reports showed the effectiveness of ELS, such evidence is scarce,^{5,6} and there is no recommendation for the use of ELS at present.^{1,18,19} In addition, ELS would need many medical personnel and resources for emergency settings, and it might be difficult to conduct ELS at all hours of the day and night even in CCMCs. The effectiveness and cost-effectiveness of ELS for OHCA patients remains a matter of debate, and this evidence should be reported from Japan where ELS is relatively common.

In Japan, both amiodarone and nifekalant have generally been available at CCMCs. Two prospective randomized studies showed that use of amiodarone improved survival until hospital admission, and amiodarone became a first-line anti-arrhythmic agent for refractory VF/pulseless VT.^{23,24} In Japan, nifekalant, another class III anti-arrhythmic agent for refractory VT and VF, has been available since 1999, and some studies have indicated its effectiveness in emergency settings.^{25,26} Further studies into what kind of anti-arrhythmic agent would be effective for shock-resistant VF should be undertaken.

In this study, 44% of out-of-hospital VF patients were transported to CCMCs. Previously, we reported that approximately 30% of OHCA patients transported to the CCMCs in

Osaka, and the proportion of witnessed cases and VF tended to be greater in the CCMC group.⁴ Because VF cases should be considered to have the best chance of survival, the greater proportion of those who were transported to the CCMCs than in a previous report involving non-VF or non-witnessed cases might suggest that the ambulance crews were likely to choose the CCMCs for such cases with the best chance of survival. Consistent with previous reports showing the effectiveness of cardiac arrest centers,²⁷ our previous report showed that survival after OHCA was better in those who were transported to CCMCs rather than non-CCMC hospitals if they did not achieve field ROSC, however, there was no information on what kind of treatments were provided. Because our medical resources are limited, we should consider the effective transportation strategy to the CCMCs or advance treatments that would lead to improved survival after VF in the area, by establishing a registry including hospital care.

The present study also suggested that the decision for TOR might differ with the institution even among CCMCs in the same area. In Japan, EMS personnel are not legally permitted to terminate resuscitation for OHCA patients in the prehospital setting. Therefore, EMS personnel in Japan are required to transport almost all OHCA patients to a hospital regardless of the success or failure of their resuscitation efforts.²⁸ Studies on the TOR rule in the prehospital settings have been carried out,^{29,30} but there are no definitive criteria for in-hospital TOR. One study suggested that the increased duration of in-hospital resuscitation efforts was associated with the improved outcome after in-hospital cardiac arrests.³¹ In the present study, some cases with very prolonged resuscitation yielded neurologically favorable survival. Therefore, further studies are required to assess the appropriate resuscitation duration or TOR rule for OHCA patients after hospital arrival.

By collecting further data on OHCA patients, we could formulate criteria for transportation to hospitals in line with each patient's condition. Indeed, we have launched a large multicenter cohort to verify the effectiveness of in-hospital advanced treatments such as the use of drugs, ELS, PCI, and TH for OHCA patients in order to determine their prognostic factors.³² We believe that this new prospective cohort would contribute to the improvement of outcomes after OHCA, including shock-resistant VF. Further evidence to evaluate the effect of advanced treatments should be accumulated in order to build a uniform protocol that can be used in all hospitals including CCMCs.

Study limitations

As with any study, there are several limitations that deserve mention. First, we did not obtain data on all prehospital shock-resistant VF patients in Osaka, and could not assess

actual treatments in emergency hospitals excluding CCMCs. A second limitation was the lack of data on the hospital performance, such as the number of staff and the emergency PCI availability. Third, we did not collect data on continuous electrocardiographic changes. These would be important to assess the timing and effect of drug administration. Finally, there might be regional variations in the transportation and treatment of OHCA patients between CCMCs in Japan.³³

CONCLUSIONS

THIS PILOT DESCRIPTIVE study suggested that the actual treatments for VF patients differed among CCMCs. Further studies are warranted to evaluate the effectiveness of in-hospital advanced treatments for VF, including shock-resistant VF patients.

CONFLICT OF INTEREST

NONE.

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